CLAIMS

WE CLAIM,

1. A method of inhibiting atrophy or inducing hypertrophy in skeletal muscle cells comprising treating the cells with an inhibitor of the SHIP2 pathway.

2. The method of claim 1 wherein the inhibitor is an inhibitor of SHIP2.

3. The method of claim 1 wherein the inhibitor of SHIP2 causes phosphorylation of Akt.

4. The method claim 1 wherein the inhibitor of the SHIP2 pathway is an activator of Akt.

5. A method of inhibiting atrophy in skeletal muscle cells comprising treating the cells with a muscle tissue-specific activator of the PI3K/Akt pathway.

6. The method of any one of claims 1, 2, 3, 4, or 5 wherein the skeletal muscle cells are in a vertebrate animal having an atrophy-inducing condition.

7. The method of claim 6 wherein the vertebrate animal is a chicken, rodent, rabbit, dog, cat, cow, horse, pig, sheep, primate, or human.

8. The method of claim 6 wherein the vertebrate animal is treated prior to exposure to or onset of the atrophy-inducing condition.

9. The method of claim 6 wherein the atrophy-inducing condition is immobilization, denervation, starvation, nutritional deficiency, metabolic stress, diabetes, aging, muscular dystrophy, AIDS/HIV infection, cancer, bed rest or myopathy.

10. A method of identifying a test agent that inhibits muscle atrophy or induces hypertrophy comprising:

(a) obtaining cells that express the following:

1) SHIP2;

2) an Akt substrate/reporter construct capable of measuring Akt pathway activation;

(b) subjecting the cells to a test agent;

(c) measuring the amount of Akt pathway activation, wherein activation of the Akt pathway is used to identify a test agent that inhibits atrophy.

11. The method of claim 10 wherein the cells are fibroblasts.

12. The method of claim 10 wherein the cells are muscle cells.

13. The method of claim 12 wherein the muscle cells are myoblasts.

14. The method of claim 13 wherein the myoblasts are C2C12 cells.

15. A method of reducing muscle atrophy or inducing muscle hypertrophy in skeletal muscle cells comprising treating the cells with an activator of the PI3K/Akt pathway.

16. The method of claim 15 wherein the activator is a specific activator of Akt.

17. The method of claim 15 wherein the activator causes phosphorylation of Akt substrates, such as mTOR, forkhead, or GSK3.

18. A method of reducing muscle atrophy or inducing muscle hypertrophy in skeletal muscle cells comprising treating the cells with a muscle tissue-specific activator of the PI3K/Akt pathway.

19. A method of reducing muscle atrophy or inducing muscle hypertrophy in skeletal muscle cells comprising treating the cells with a muscle tissue-specific inhibitor of the SHIP2 pathway.

20. A method of reducing muscle atrophy or inducing muscle hypertrophy in skeletal muscle cells comprising treating the cells with an inhibitor of the SHIP2 pathway.

21. A method of reducing muscle atrophy or inducing muscle hypertrophy in skeletal muscle cells comprising treating the cells with an inhibitor of SHIP2.

22. The method of any one of claims 15, 18, 19, 20, or 21, wherein the skeletal muscle cells are within a vertebrate animal.

23. The method of claim 22 wherein the vertebrate animal is a chicken, rodent, rabbit, dog, cat, cow, horse, pig, sheep, primate, or human.

24. A cell comprising:

1) SHIP2;

2) an Akt substrate/reporter construct capable of measuring Akt substrate activation.

25. A SHIP2 antagonist for use in a method of inhibiting atrophy, inducing hypertrophy, activating the Akt pathway, interfering with the calcineurin pathway, or modulating Akt expression or activity.

26. A method of screening compounds useful for the treatment of muscle atrophy or detecting atrophy and related diseases and disorders comprising contacting a muscle cell expressing SHIP2 with a compound and detecting a change in the SHIP2 protein activity or the Akt pathway.

27. The method of claim 26 wherein the change is measured by PCR, Taqman PCR, phage display systems, gel electrophoresis, yeast-two hybrid assay, Northern or Western analysis, immunohistochemistry, a conventional scintillation camera, a gamma camera, a rectilinear scanner, a PET scanner, a SPECT scanner, a MRI scanner, a NMR scanner, or an X-ray machine.

28. The method of claim 26 where in the change in SHIP2 protein activity is detected by detecting a change in the interaction of SHIP2 with one or more proteins, by

detecting a change in the interaction of Akt with another protein, or by detecting a change in the level of one or more of the proteins in the Akt pathway.

29. The method of claim 26 wherein the muscle cell is of skeletal muscle origin.

30. The method of claim 26 wherein the muscle cells are cultured cells.

31. The method of claim 26 wherein the muscle cells are obtained from a transgenic organism.

32. The method of claim 31 wherein the transgenic organism includes, but is not limited to a mouse, rat, rabbit, sheep, cow or primate.

33. The method of claim 26 wherein the muscle cells are within a transgenic organism.

34. The method of claim 33 wherein the transgenic organism includes, but is not limited to a mouse, rat, rabbit, sheep, cow or primate.

35. A method of detecting muscle atrophy in an animal comprising measuring SHIP2 in a patient sample.

36. A method of inhibiting atrophy or inducing hypertrophy by modulating SHIP2.

37. A method of treating illnesses, syndromes or disorders associated with muscle atrophy comprising administering to an animal a compound that modulates SHIP2 or the Akt pathway such that symptoms are alleviated.

38. The method of claim 37 such that the animal is a mammal.

39. The method of claim 37 such that the mammal is a human.

40. A method of identifying a test agent capable of inhibiting muscle atrophy or inducing muscle hypertrophy in vitro comprising:

(a) contacting a mixture containing SHIP2 and phosphatidylinositol 3,4,5-trisphosphate with a test agent; and

(b) measuring the ability of SHIP2 to mediate the conversion of phosphatidylinositol 3,4,5-trisphosphate.

41. The method of claim 40 wherein such measuring is accomplished either by measuring the release of the phosphate at the "5" position, or by determining the amount of residual phosphatidylinositol 3,4,5-trisphosphate or measuring binding of a phosphotidylinositol-3,4,5-trisphosphate-specific agent to phosphotidylinositol-3,4,5-trisphosphate.

42. The method of claims 41 such that the phosphotidylinositol-3,4,5-trisphosphate-specific agent is Akt.

43. The method of claim 40 wherein such measuring is accomplished by fluorescence, PCR, Taqman PCR, phage display systems, gel electrophoresis, yeast-two hybrid assay, Northern or Western analysis, immunohistochemistry, a conventional scintillation camera, a gamma camera, a rectilinear scanner, a PET scanner, a SPECT scanner, a MRI scanner, a NMR scanner, or an X-ray machine

44. The method of claim 40 wherein such test agent is a carbohydrate, a lipid, a protein, a salt, a nucleic acid, or a small molecule.